Attorney Docket No. SAIC-0062CON-1
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	)	
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R. Paul Schaudies, et al.	)	
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Serial No. **10/630,384**	)	Art Unit: **1637**
	)	
Filed: **JULY 30, 2003**	)	Examiner:
	)	
For: **METHOD FOR DETECTING A BIOLOGICAL ENTITY IN A SAMPLE**	)	
	)	

DECLARATION BY R. PAUL SCHAUDIES AND DOREEN A. ROBINSON UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1430

Sir:

1. I, R. Paul Schaudies, Ph.D., a co-inventor of the above-identified patent application, do hereby declare that I received a Doctor of Philosophy degree in Biochemistry from Temple University School of Medicine in 1985; worked as an Investigator in the Department of Clinical Investigation and as a Senior Scientist in the Department of Nephrology at Walter Reed Army Medical Center in Washington, D.C.; and worked as a Program Manager in the Central Measurement and Signature Intelligence Office, Chemical and Biological Collection Systems Division, at the Defense Intelligence Agency in Washington, D.C.

I am currently Assistant Vice President and Division Manager for Biological and Chemical Defense at Science Applications International Corporation. In this position, I established procedures used in the *Bacillus anthracis* decontamination of federal buildings in Washington, D.C following the anthrax attack in 2001, including the mailrooms of the Dirksen and Ford Office Buildings and the Hart Senate Office Building.

I am currently serving on three National Academy of Sciences studies to evaluate biological sensing systems (nanotechnology, biosensing systems and building decontamination standards); have been Vice-Chair and Corresponding-Chair of two Gordon Research Conferences on defense against chemical and biological terrorism; have served on national panels providing scientific guidance in the areas of chemical and biological detection technologies, wireless networks, and biological remediation technologies for Defense Advanced Research Projects Agency (DARPA) and the Department of Energy; have served as an outside reviewer of scientific proposals for the Chemical and Biological Nonproliferation Program of the Department of Energy; and have served as a United Nations Inspector for biological weapons in Iraq.

2. I, Doreen A. Robinson, Ph.D., a co-inventor of the above-identified patent application, do hereby declare that I received a Doctor of Philosophy degree in Biochemical Pharmacology from University of Buffalo, Buffalo, New York in 1988 (J. Craig Venter (thesis advisor)); worked as a research scientist at the National Institutes of Health, National Institute for Neurological Disorders and Stroke in Bethesda, Maryland; and worked as an Intelligence Officer at the Central Intelligence Agency in Washington, D.C. I am currently Scientific Program Manager for Biological and Chemical Defense at Science Applications International Corporation. In this capacity, I participated in the *Bacillus anthracis* decontamination of several federal buildings in Washington, D.C. as described above.

3. We, R. Paul Schaudies, Ph.D. and Doreen A. Robinson, Ph.D., do hereby further declare that a critical and long felt need has existed for broad spectrum, high confidence biological warfare agent detection and identification methods and that the methods described in the above-identified patent application resolve this long felt need.

a. <u>The need for a broad spectrum, high confidence biological detection and identification system has existed for over 50 years.</u>

The need for rapid, accurate methods to track the source and spread of infectious disease, including that initiated through acts of bioterrorism and biological warfare attacks against the U.S. military, has been a U.S. priority for over 50 years. In fact, the Epidemic Intelligence Service of the Centers for Disease Control and Prevention (CDC)

was founded in 1951 in response to concerns over the possibility of a covert biological attack within the United States.[1] This fact points to a long felt need for improved tools to detect a biological attack and to facilitate epidemiological tracking. Regardless of intent, it is important for epidemiologists to be able to identify and characterize the strains of disease-causing agents in an outbreak or epidemic in order to determine the source and mechanisms of spread and, thus, to limit the effects of present and future outbreaks. The detection methods described in the above-identified patent application will greatly improve detection, identification and characterization of biological warfare agents as well as epidemiological analysis of outbreaks resulting from intentional attacks or natural outbreaks, from rapidly recognizing sentinel cases to tracking the spread and source of disease.

The threat of biological weapons in modern warfare arose in World War I when German agents were suspected of inoculating U.S. horses and cattle with Glanders, a serious bacterial disease of the respiratory tract and skin. Japan embarked on an ambitious biological warfare program in 1937, and the U.S. and several other nations initiated programs during World War II. The U.S. offensive program was disestablished in 1969, but the U.S. defensive biological warfare program has remained strong due to a continued threat from Russia and several other nations suspected of continuing to pursue offensive biological warfare programs.

The U.S. Army's Edgewood Chemical and Biological Center (ECBC) has been a leader in the development of devices to protect our armed forces against biological or chemical attack. ECBC standardized the Army's first biological agent sampling kit in 1957 and the first decontaminating agent against biological agents in 1960. In 1974, ECBC began development of a biological detection and warning system to respond to a critical need to field a biological agent detection system. These developments, along with various suspected instances of the use of biological agents in the 20th century, demonstrate a long felt need for a rapid, reliable technology capable of identifying a broad spectrum of biological attack agents available to U.S. enemies. Methods are

[1] Technical Aspects of Biological Weapon Proliferation, Federation of American Scientists, Special Weapons Primer, p. 107. **www.fas.org/nuke/intro/bw/**, **fas.org/spp/starwars/ota/934405/pdf**.

available for the detection of a few biological agents, but vulnerability exists to hundreds of other pathogens that could be used as biological weapons. In addition, systems developed over the past 30 years are extremely limited in terms of throughput. They are not well suited for individual or collective protection of military forces or homeland civilian population because they are bulky systems that are costly to purchase and operate, are reagent and manpower intensive, and have high power requirements.

The first recognized major biological warfare attack in the United States was organized in 1984 by a religious cult in Oregon who poisoned food at local restaurants with *Salmonella typhimurium* in an attempt to influence the outcome of a political election by incapacitating anti-cult voters.[2] Scientists investigating the numerous reports of food poisonings never thought to consider bioterrorism as a probable cause of the mysterious illness, and no biological warfare detection methods were available to them to make such a determination.

By 1991, although scientists recognized the need to develop biological warfare detection methods, the only proposed solution was to use **available** laboratory technologies on **massive** scales. Scientists stated, "[m]itigating the threat of bio-attacks will likely demand high-throughput laboratory detection and characterization capabilities on **unprecedented scales**."[3] This "brute force" approach was found to be both costly and labor intensive.

Seven years later, in 1998, the need was still unresolved and new, improved ideas were still lacking. Articles continued to call for the use of intensive technologies on grand scales, making statements such as, "Mitigating the threats posed by biological weapons and terrorism will demand **massive** laboratory detection and characterization capabilities."[4] This particular article further stated that "[s]o-called traditional laboratories would be **incapable of answering even the most fundamental questions**"

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[2] Miller *et al.*, GERMS: BIOLOGICAL WEAPONS AND AMERICA'S SECRET WAR, pp. 15-33, Simon & Schuster, New York, 2001.
[3] Patel *et al.*, Automation in Threat Reduction and Infectious Disease Research: Needs and New Directions, *J. Association for Lab. Automation* 4(1):51-54 1991, emphasis added.
[4] Scott Layne and Tony Beugelsdijk, Laboratory Firepower for Infectious Disease Research, *Nature Biotechnology*, 16:825-829, 825 1998.

about a biological warfare agent following a bio-attack.[5] Instead of providing a single method that could answer enormous numbers of questions and thereby accurately detect, identify and characterize a biological agent in a sample, the article merely provides a suggestion to use the Internet to increase the amount of data shared between scientists.[6] Therefore, the solutions proposed by 1998 continued to require a "Herculean effort" involving the use of costly and labor intensive methodologies on a massive scale.

Vulnerability to biological attack was clearly illustrated by delivery of a series of anthrax-laced letters by the U.S. Postal Service in the fall of 2001. The handling of these letters resulted in five deaths and illness in several other individuals. This episode in U.S. history was a real wake-up call that pointed out to U.S. leaders and citizens alike the disruption and damage that can result from a biological attack using small amounts of material and extremely simple delivery methods. If not for the training of Capitol Hill employees, the overt delivery method utilized by the perpetrator, and the rapid implementation of prophylaxis procedures, it is highly likely that many more deaths could have resulted. In terms of economic cost, the Capitol Hill clean-up is estimated to have cost at least $40 million. The cost to clean-up the Brentwood Postal Facility is estimated to be far higher, over $200 million, with a down time of over two years.

The dramatic human and economic costs of a biological attack were pointed out by Kaufmann *et al.*[7] even before the events of 2001. In a 1997 paper, the authors developed a model that calculated that the economic impact of a bioterrorist attack could reach $26.2 billion per 100,000 persons exposed to anthrax. The authors concluded that rapid implementation of prophylaxis was the single most important parameter for reducing the impact of such an attack. Therefore, methods must be found to decrease the time and cost of recovery from such an event. The detection methods described in the above-identified patent application, which has the ability to rapidly and accurately screen for all known pathogens simultaneously in the course of hours, will dramatically increase

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[5] *Id.*, emphasis added
[6] *Id.* at 826.
[7] The Economic Impact of a Bioterrorist Attack: Are Prevention and Postattack Intervention Programs Justifiable? Arnold F. Kaufmann, Martin I. Meltzer, and George P. Schmidt, *Emerging Infectious Diseases*, Vol. 3, No. 2, April-June 1997, pp. 83- 94.

our nation's effectiveness to recognize, respond to and mitigate such an event by allowing rapid implementation of prophylaxis.

After the anthrax incident, scientific leaders continued to grapple with the issue of how to respond to a biological attack. In 2001, the Defense Science Board (DSB) conducted a study that focused on ways to improve the speed, breadth, and accuracy of clinical diagnosis in order to recognize and react to a biological attack. The Board recommended development of a "Zebra Chip" to help distinguish a sentinel case of a biological attack from more common infections. In other words, it was recognized that technology was needed to distinguish "zebras" from "horses". The reference to zebras and horses refers to an analogy used to teach medics. It refers to the fact that common diseases are, by definition, the most frequent. Thus, if a physician hears hoof beats, it is more likely to be a horse than a zebra. The term "Zebra Chip" was coined to represent a methodology or technology that can identify the occasional zebra amongst this thundering herd of horses.

In a presentation given by Dr. George Poste, chair of the DSB's study, Dr. Poste summarized the recommendations of the DSB for strengthening U.S. capabilities to mitigate a biological attack. Dr. Poste noted that seven of the eight top bioagents that could be used as biological weapons would, in fact, present with similar symptoms that are common to those of influenza. Dr. Poste provided evidence to support the feasibility of multiple scenarios involving genetically engineered and "hybrid" viruses and bacteria that dictate the need for a wide spectrum of defense postures. He made the point that faster identification saves lives, and that this requires rapid and accurate diagnosis of infection in people because this is how we are most likely to recognize a covert biological attack.

The DSB emphasized that better ways of identifying or "fingerprinting" biological agents and exploiting that information to build improved diagnostic tests were needed. The DSB viewed the "Zebra Chip" as building on advances that are occurring in miniaturization technologies that can immobilize oligonucleotides representing pathogen target sequences onto chips to profile those organisms, including characteristics associated with their virulence, and in this case microbial genes are profiled. The idea is

to create a comprehensive genomic and proteomic profile to identify conventional and unconventional biological agents and to put that profile onto chips.[8]

More recently, intelligence sources indicated that a potentially dangerous biological agent may have been present in a container on a ship bound for the port of Newark, NJ. Officials were shocked to find out that the strike team sent to respond could only test in the field for the presence of three biological agents. The CDC's Laboratory Response Network could test for less than 10 agents, and the state-of-the-art Biological Forensics Analysis Center could determine the presence of 20 agents only after performing tests that took weeks.

Today, twenty years and several biological attacks after the first recognized bioterrorist event in the United States, no rapid, reliable, broad spectrum, high confidence, biological identification or characterization systems exist that yield low false positive detection rates. Biological warfare agents are still likely to be detected only after widespread illness or even death. The potential for massive numbers of sick or dead has only increased as biowarfare researchers have learned to genetically modify biological warfare agents to increase their virulence, infectivity and transmissibility. Today more than ever, rapid biological detection methods are needed.

b. The search for biological weapons detection methods has been expensive.

Although scientists and military personnel recognized the need for a biological weapons detection method long before the anthrax attack of 2001, they have failed in their search for a useful detection method that fulfills existing requirements regarding confidence, multiplexing, the ability to characterize unknown organisms and the ability to provide indications of genetic manipulation. This search for rapid and accurate biological weapons detection methods has been expensive and has led the United States to spend considerable funds on research related to and including such methods. During at least the last six years, the United States Government has steadily increased the amount of appropriations made to programs such as the U.S. Department of Defense Chemical and

[8] ADVANCES IN BIOTECHNOLOGY: PROMISE AND PERIL, George Poste, Ph.D. **http://www.upmc-biosecurity.org/pages/events/2nd_symposia/transcripts/trans_post.html**

Biological Defense Program.[9] The appropriations made to this program reached an unprecedented estimated amount of **$1.3 billion** in the year 2003.[10] The President has committed billions of dollars to the BioWatch and BioShield programs in order to improve our capability as a nation to recognize and respond to a biological attack. The detection methods described in the above-identified patent application can dramatically improve our nation's ability to recognize and contain outbreaks and epidemics resulting from a biological attack or from the introduction of emerging or reemerging diseases.

c. Currently available biological detection methods are inadequate.

Current biological detection and identification methods can only look for one, or a few, unique DNA sequences for a particular organism in a single assay. False positive rates in these systems are quite high (greater than 1 in 10^4). Thus, confirmatory tests that can take hours to days are required to increase the confidence that contamination or infection with a particular agent has actually occurred. Moreover, fielded systems for the military and civilian bioterrorism defense are capable of identifying a limited number of the top threat agents (about 10). This is only about 10% of the combined HHS and USDA select agent lists of biological agents deemed to pose a grave threat to U.S. persons, livestock and economically important plants. Finally, most of the top threat agents present with highly similar symptoms in the early stages of disease and most of the top threats are not commonly encountered in developed countries. Thus, our medical professionals are not trained or experienced in recognition and differential diagnosis of these agents. These facts clearly illustrate a gaping hole in our nation's defense against militarily relevant threats as well as terrorist attacks on our civilian population. The detection methods described in the above-identified patent application will allow military and civilian personnel to monitor the presence of all relevant threat agents simultaneously with high confidence. Additionally, these methods will enable personnel to detect and characterize unknown or unexpected threats and to identify signs of genetic engineering.

A comprehensive environmental monitoring system to protect the U.S. against such threats is not economically or technically feasible. Thus, experts espouse the need to

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[9] Department of Defense Chemical and Biological Defense Program Annual Report to Congress, vol. 2, page G-2.
[10] *Id.*

integrate surveillance and preparation to mitigate the bioterrorist threat with an enhanced public health infrastructure that will improve our ability to detect and rapidly react to emerging or reemerging diseases such as SARS or Rift Valley Fever. The virulence and high transmissibility of the SARS virus has been clearly documented in numerous lay and scientific publications. A rapid method to classify and isolate persons infected with the SARS virus is paramount in terms of limiting the spread of infection and mitigating the human and economic costs. During such an outbreak, it is not even critical that diagnostic devices and methods taxonomically classify the causative agent so long as they can accurately distinguish individuals infected with the virulent agent from those with more common infections. The highly multiplexed approach for simultaneously monitoring a broad spectrum of biological agents described in the above-identified patent application will provide this capability through taxonomic classification and pattern recognition.

Forensics is another area of need for a highly multiplexed biological identification and characterization capability. FBI scientists are in need of rapid methods to assess the validity of innumerable threats of biological contamination and exposure that they encounter on a daily basis. A Monterey Institute article in the summer of 2000 chronicled some of the biological threats that have come to public attention in recent years. For example, the authors of the article found 175 WMD incidents in 1999.[11] Of these, 56.5% were biological threats that turned out to be hoaxes. The technology described in the above-identified patent application will enable FBI scientists and field operatives to rapidly distinguish a real threat from a hoax, even in the case where one agent is declared or assumed but another is actually present.

d. Methods for monitoring intelligence and treaty compliance are needed.

A major concern in the arena of biological warfare is the ability to use "dual use" facilities to clandestinely produce toxic biological agents. The detection methods

[11] Cameron G., Pate J., McCauley D. and DeFazio L. 1999 WMD Terrorism Chronology: Incidents Involving Sub-National Actors and Chemical, Biological, Radiological, and Nuclear Materials. The Nonproliferation Review/Summer 2000, pp. 157-174.
http://cns.miis.edu/pubs/npr/vol07/72/wmdchr72.htm

described in the above-identified patent application may be useful for monitoring surfaces inside a facility, effluents or the surrounding environment to characterize the biological agents and possibly even the production schedule being used in a particular facility.

The elusiveness of rapid and accurate methods for the detection of biological warfare agents is largely attributable to the fact that both rapid and accurate detection requires that **multiple questions about a sample be answered simultaneously**. For example, when testing a biological sample for the presence of a biological warfare agent, it should be determined if there are one or more biological entities in the sample, whether the biological entity is a virus, a bacteria or some other type of pathogen, whether the particular strain or type of biological entity is one previously characterized or known, whether the particular strain or type of biological entity is virulent, whether the biological entity contains DNA sequences from other biological entities that may affect its virulence, etc. The questions are numerous and the answers must be accurate since mischaracterization of the biological entity can result in the death of thousands.

e. Recent legislation requires sophisticated detection methods to ensure compliance.

The impact on and response to the incidents of 2001 by U.S. policy makers is illustrated by DHHS 42 CFR Part 73 (Nov. 3, 2003) entitled "Possession, Use, and Transfer of Select Agents and Toxins", which amends an interim final rule published on Dec. 13, 2002, that established requirements regarding possession and use in the U.S., receipt from outside the U.S., and transfer within the U.S., of select agents and toxins. The requirements were established to implement provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188. The Act bolstered the authority of the Secretary of DHHS to protect the American public against the misuse of select agents and toxins whether inadvertent or the result of terrorist acts against the U.S. homeland (such as the recent terrorist acts involving anthrax) or other criminal acts. The act gave to the Secretary broad discretion in establishing and enforcing the new regulations to ensure that select agents and toxins would remain available for research, education, and other legitimate purposes. The act also gave the USDA the

authority and responsibility for regulating activities regarding select agents and toxins to protect animal and plant health and animal and plant products. The act gave the Secretary of HHS the authority and responsibility for regulating activities regarding select agents and toxins to protect the public health and safety. Some of the select agents and toxins regulated under the HHS Dec. 2002 interim final rule are also regulated by USDA under 9 CFR part 121. The select agents and toxins subject to regulation by both agencies are identified as "overlap" select agents and toxins and those regulated solely by HHS are identified as HHS select agents and toxins. The lists contains more than 80 biological agents of concern: 29 HHS Non-Overlap Select Agents and Toxins, 20 High Consequence Livestock Pathogens and Toxins/Select Agents (Overlap Agents), 23 USDA High Consequence Livestock Pathogens and Toxins (Non-Overlap Agents and Toxins) and 10 Listed Plant Pathogens. The detection methods described in the above-identified patent application may be used to simultaneously monitor for the presence of all of these agents.

f. The methods described in the above-identified application satisfy the long felt need.

Prior to the methods described in the above-identified patent application, **no satisfactory technologies existed** for the detection of biological warfare agents having broad spectrum, high confidence, identification or characterization systems that yield low false positive detection rates. The methods described in the above-identified patent application resolve this long-felt and critical need for the first time. The methods combine nucleic acid sequences in the sample with multiple primers of randomized nucleotide sequences, amplify the nucleic acid sequences, and hybridize the amplification products to an array of predetermined nucleic acids. These methods, **unlike any prior methods**, are capable of satisfactorily answering numerous questions about a sample simultaneously with a high degree of confidence. The methods also allow one to determine key functional information such as virulence factors and antibiotic resistance along with phylogenetic information about a biological entity even when the exact identity of the entity cannot be ascertained and can provide indications of genetic manipulation of the biological entity.

The above-identified application satisfies a long felt need by providing methods for detecting one or more biological entities in a sample and for obtaining information resident in the genetic code of a biological entity in a sample. The methods are particularly useful for the detection or characterization of a pathogen, such as a biological weapon. The ability to identify an organism using hundreds of specific probes simultaneously will make false positives a phenomenon of the past. The methods described in the above-identified application are useful for simultaneously determining the presence or absence of thousands of informative nucleic acid sequences from an entire sample, thereby providing rapid, meaningful results. The methods of the above-identified application are specific, yet have minimal false positive results, thereby providing a high degree of confidence in the results obtained because of the high magnitude of genetic sequence and related information than can be provided simultaneously. Furthermore, the methods of the above-identified application can be used to identify signs of genetic engineering in an organism, can characterize unknown or previously unidentified organisms, and can provide information concerning virulence, antibiotic resistance or other DNA features of the biological entity. Clearly, such methods are seriously needed.

Because the methods described in the above-identified patent application do **not** require the use of traditional laboratory techniques on unprecedented scales, they provides for the **first time** satisfactory methods for detecting biological agents such biological warfare agents in a sample and resolve the critical and long felt need for such methods.

4. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of any patent issuing on this application.

18 October 2004
Date

R. Paul Schaudies

18 October 2004
Date

Doreen A. Robinson

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	)	
	)	
R. Paul Schaudies, et al.	)	
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Serial No. **10/630,384**	)	Art Unit: **1637**
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	)	
For: **METHOD FOR DETECTING A BIOLOGICAL ENTITY IN A SAMPLE**	)	

STATEMENT BY R. PAUL SCHAUDIES AND DOREEN A. ROBINSON IN SUPPORT OF PETITION TO MAKE SPECIAL

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1430

Sir:

1. We, R. Paul Schaudies, Ph.D. and Doreen A. Robinson, Ph.D., do hereby declare that we are co-inventors of the above-identified patent application, which is directed to a method for detecting one or more biological entities in a sample and for obtaining information resident in the genetic code of a biological entity in a sample. The method is particularly useful for the rapid detection or characterization of one or more pathogens being used as biological weapons. In addition, the method can be used to identify signs of genetic engineering in the biological entity, can characterize unknown or previously unidentified biological entities, and can provide information concerning

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on Oct. 29, 2004.

Jamie L. Greene – Reg. No. 32,467

virulence, antibiotic resistance or other DNA features of the biological entity, all of which are useful in countering biological weapons.

2. We further declare that, because biological weapons are dangerous to human life and have been used by terrorists to intimidate or coerce a civilian population or to intimidate or coerce the policy of a government, the invention described in the above-identified patent application relates to a counter-terrorism invention within the meaning of M.P.E.P. §708.02 XI (Inventions for Countering Terrorism) as described in more detail below. Therefore, we request that the above-identified application be made "special" by the U.S. Patent and Trademark Office. A Petition to Make Special under 37 C.F.R. §1.102(b) is enclosed.

3. Terrorists use a wide variety of weapons, including biological weapons. Biological weapons are weapons that cause infectious disease in humans, which can be debilitating or deadly. For example, an explosive device that releases a pathogen into the environment when detonated is a biological weapon intended to infect a vast number of individuals at once. In the case of a communicable disease such as smallpox or plague, the infected individuals spread the disease to others, thereby causing widespread sickness or death. However, because a pathogen is a living organism that, once it has been introduced into a population can be spread rapidly from one individual to another, a pathogen could be introduced into the environment by many unnoticed means, such as through air ventilation systems, by water contamination, or by the direct infection of one human or animal who then is released into the general population to infect others.

4. In a situation where a terrorist act involving biological agents has taken place, the pathogen first must be detected so that healthcare workers will be able to rapidly implement protective measures such as containment of the pathogen to prevent further spread of disease, isolation and treatment of infected individuals, administration

of vaccines or therapeutic agents (if available), and the safe decontamination of infectious environments or locations. The pathogen should also be identified and characterized so that the workers will know how to contain and remove the pathogen, treat those who have been infected, and protect those who are at risk of becoming infected. The above-identified patent application provides technology for both detecting, identifying and characterizing pathogens that could be used in biological weapons by terrorists. Therefore, the above-identified patent application is useful for countering bioterrorism.

5. The events of Sept. 11, 2001 reinforced the need to enhance the security of the United States. The anthrax attacks that followed demonstrated the feasibility of bioterrorism and the cost in terms of human lives and disruption of government as well as dollars. Congress responded by passing the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the Bioterrorism Act), which President Bush signed into law June 12, 2002. Section 126 of the Bioterrorism Act (excerpt provided below) specifically addresses the evaluation of new and emerging technologies:

> SEC. 126. EVALUATION OF NEW AND EMERGING TECHNOLOGIES REGARDING BIOTERRORIST ATTACK AND OTHER PUBLIC HEALTH EMERGENCIES.
>
> (a) In General.--The Secretary of Health and Human Services (referred to in this section as the "Secretary") shall **promptly** carry out a program to periodically evaluate new and emerging technologies that, in the determination of the Secretary, are designed to improve or enhance the ability of public health or safety officials to conduct public health surveillance activities relating to a bioterrorist attack or other public health emergency.
>
> (b) Certain Activities.--In carrying out this subsection, the Secretary shall, to the extent practicable--(1) survey existing technology programs funded by the Federal Government for potentially useful technologies; (2) **promptly** issue a request, as necessary, for information from non-Federal public and private entities for ongoing activities in this area; and (3) evaluate technologies identified under paragraphs (1) and (2) pursuant to subsection (c).
>
> (c) Consultation and Evaluation.--In carrying out subsection (b)(3), the Secretary shall consult with the working group under section 319F(a) of the Public Health Service Act, as well as other appropriate public,

> nonprofit, and private entities, to develop criteria for the evaluation of such technologies and to conduct such evaluations.
> (d) Report.--**Not later than 180 days after the date of the enactment of this Act,** and periodically thereafter, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives, and the Committee on Health, Education, Labor, and Pensions of the Senate, a report on the activities under this section.
> (emphasis added)

As emphasized in the Act, there is an immediate demand for the development of advanced technology to address the potential threat of a bioterrorist act.

6. During at least the last seven years, the United States Government has steadily increased the amount of appropriations made to programs such as the U.S. Department of Defense Chemical and Biological Defense Program. (Department of Defense Chemical and Biological Defense Program Annual Report to Congress, vol. 2,) The appropriations made to this program reached an unprecedented estimated amount of **$1.3 billion** in the year 2003. (*Id.*)

7. The commitment of the United States government in responding to bioterrorism is further evidenced by the Pentagon's support of DARPA (Defense Advanced Research Projects Agency). In the late 1990's, the Pentagon dramatically increased funding for DARPA in an effort to find new ways of fighting infectious disease. The annual budget went from $59 million in 1998 to $162 million in 2001, and is projected to exceed $205 million by 2005. Over this period, DARPA is expected to spend approximately $1.2 billion in total working toward the goal of developing novel medical treatments and researching devices such as germ detectors. (http://www.pbs.org/wgbh/nova/bioterro/germs.html (Miller *et al.*, GERMS: BIOLOGICAL WEAPONS AND AMERICA'S SECRET WAR, Simon & Schuster, New York, 2001.))

8. Currently, no rapid, reliable, pathogen identification or characterization methods exist that yield broad spectrum, low false positive detection rates. Biological warfare agents are likely to be detected only after widespread illness or even death. The

potential for massive numbers of sick or dead has only increased as biowarfare researchers have learned to genetically modify biological warfare agents to increase their virulence, infectivity and transmissibility. Today more than ever, rapid pathogen detection methods are needed, especially those that can identify signs of genetic engineering and to characterize unknown pathogens, such as the technology described in the above-referenced patent application.

9. The events of the past few years have demonstrated the reality of terrorist attacks on United States soil. As discussed above, the United States government has recognized the importance of continuing to develop counter terrorist measures and weapons, and now it has highlighted the importance to do so at a faster rate. The invention described in the above-referenced patent application uniquely addresses crucial and initial aspects of addressing bioterrorism: the detection, identification and characterization of the biological agents used as a biowarfare agents. The invention is useful as a tool against national and international terrorism, specifically terrorism that includes activities that involve violent acts or acts dangerous to human life, as well as activities that appear to be intended to intimidate or coerce a civilian population, to influence the policy of a government by intimidation or coercion, or to affect the conduct of a government by assassination. Accordingly, applicants request that the above-identified patent application be made "special" and examination expedited.

10. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of any patent issuing on the above-identified application.

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